

From the INTERNATIONAL SEARCHING AUTHORITY

To:
 RIDOUT & MAYBEE LLP
 Attn. McKay, Margaret H.
 150 Metcalfe Street
 Suite 1900
 Ottawa, Ontario K2P 1P1
 CANADA

PCT

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT
OR THE DECLARATION

(PCT Rule 44.1)

Date of mailing (day/month/year)	07/08/2003
-------------------------------------	------------

Applicant's or agent's file reference 42472-0011	FOR FURTHER ACTION See paragraphs 1 and 4 below
International application No. PCT/CA 03/ 00077	International filing date (day/month/year) 27/01/2003
Applicant LAUTT, Wayne, W.	

1. The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
 34, chemin des Colombettes
 1211 Geneva 20, Switzerland
 Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. Further action(s): The applicant is reminded of the following:

Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90b/s.1 and 90b/s.3, respectively, before the completion of the technical preparations for international publication.

Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority

 European Patent Office, P.B. 5818 Patentlaan 2
 NL-2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

Chantal Meyer

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

NOTE TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]: "Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]: "Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]: "Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or "Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]: "Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PATENT COOPERATION TREATY
PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 42472-0011	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/CA 03/ 00077	International filing date (day/month/year) 27/01/2003	(Earliest) Priority Date (day/month/year) 25/01/2002
Applicant LAUTT, Wayne, W.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. Certain claims were found unsearchable (See Box I).

3. Unity of invention is lacking (see Box II).

4. With regard to the **title**,

the text is approved as submitted by the applicant.

the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

the text is approved as submitted by the applicant.

the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

as suggested by the applicant.

because the applicant failed to suggest a figure.

because this figure better characterizes the invention.

1

None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 000077

A. CI IPC	IFICATION OF SUBJECT MATTER				
	A61K31/00	A61K31/40	A61K31/4166	A61K31/444	A61K31/4375
	A61K31/4709	A61K31/519	A61K31/52	A61K31/522	A61P3/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 03 028730 A (NOVARTIS AG ET AL) 10 April 2003 (2003-04-10) claims 1-9 ---	1-40
X,P	WO 02 24698 A (SCHERING CORPORATION) 28 March 2002 (2002-03-28) claims 1,31 page 92, line 7 - line 24 page 84, line 13 -page 85, line 16 --- WO 02 13798 A (PFIZER LTD ET AL) 21 February 2002 (2002-02-21) claims 1-63 --- -/-	1-4,9, 10, 17-20, 22,32-40
X,P		1-40

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
24 July 2003	07/08/2003

Name and mailing address of the ISA
 European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.
 Fax: (+31-70) 340-3016

Authorized officer

Siatou, E

INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 02/00077

C.(Co.)	action) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 1 142 879 A (FUJISAWA PHARMACEUTICAL CO. LTD.) 10 October 2001 (2001-10-10) claims 1-10 page 12, paragraph 54 ---	1-4, 9, 10, 17-20, 22, 32-40
X	EP 1 020 452 A (FUJISAWA PHARMACEUTICAL CO. LTD.) 19 July 2000 (2000-07-19) page 68, paragraph 391 claims 1-16 page 13, paragraph 45 - paragraph 47 ---	1-9, 17-20, 22-25, 28, 32-40
X	Y. NAKAYA ET AL: "Cilostazol, a phosphodiesterase inhibitor, improves insulin sensitivity in the Otsuka Long-Evans Tokushima Fatty Rat, a model of spontaneous NIDDM" DIABETES, OBESITY AND METABOLISM, vol. 1, no. 1, January 1999 (1999-01), pages 37-41, XP002248686 the whole document ---	1-5, 8, 9, 19, 20, 22-24, 32-40
A	LAUTT W W: "THE HISS STORY OVERVIEW: A NOVEL HEPATIC NEUROHUMORAL REGULATION OF PERIPHERAL INSULIN SENSITIVITY IN HEALTH AND DIABETES" CANADIAN JOURNAL OF PHYSIOLOGY AND PHARMACOLOGY, OTTAWA, ONT, CA, vol. 77, no. 8, August 1999 (1999-08), pages 553-562, XP009011015 cited in the application the whole document ---	1-40
A	PETRIE J R ET AL: "ENDOTHELIAL NITRIC OXIDE PRODUCTION AND INSULIN SENSITIVITY. A PHYSIOLOGICAL LINK WITH IMPLICATIONS FOR PATHOGENESIS OF CARDIOVASCULAR DISEASE" CIRCULATION, AMERICAN HEART ASSOCIATION, DALLAS, TX, US, vol. 93, no. 7, 1 April 1996 (1996-04-01), pages 1331-1333, XP002924506 ISSN: 0009-7322 the whole document ---	1-40
A	ALISON J. EVANS ET AL: "Insulin resistance and beta-cell dysfunction as therapeutic targets in type 2 diabetes" DIABETES, OBESITY AND METABOLISM, vol. 3, 2001, pages 219-229, XP002248687 page 224, right-hand column -page 226, left-hand column -----	1-40

INTERNATIONAL SEARCH REPORTInternational application No.
PCT/CA 03/00077**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 1, 19-40 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/CA 000077

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 03028730	A 10-04-2003	WO US 2003114469	A2 A1	10-04-2003 19-06-2003
WO 0224698	A 28-03-2002	AU CA EP NO WO US	9102201 A 2421910 A1 1319003 A1 20031238 A 0224698 A1 2002169174 A1	02-04-2002 28-03-2002 18-06-2003 14-05-2003 28-03-2002 14-11-2002
WO 0213798	A 21-02-2002	AU CA EP WO US WO US	7660701 A 2419033 A1 1307183 A2 0213798 A2 2002165237 A1 02060422 A2 2002143015 A1	25-02-2002 21-02-2002 07-05-2003 21-02-2002 07-11-2002 08-08-2002 03-10-2002
EP 1142879	A 10-10-2001	AU AU BR CA EP CN CZ HU WO TR	758325 B2 1690500 A 9917112 A 2356838 A1 1142879 A1 1335837 T 20012338 A3 0104657 A2 0039097 A1 200101865 T2	20-03-2003 31-07-2000 29-01-2002 06-07-2000 10-10-2001 13-02-2002 12-12-2001 29-05-2002 06-07-2000 21-12-2001
EP 1020452	A 19-07-2000	AU AU BR EP HU US CN WO TR TW ZA	748541 B2 7934698 A 9811273 A 1020452 A1 0002324 A2 6420409 B1 1268123 T 9900373 A1 9903277 T2 453999 B 9805598 A	06-06-2002 19-01-1999 18-07-2000 19-07-2000 28-05-2001 16-07-2002 27-09-2000 07-01-1999 21-07-2000 11-09-2001 25-01-1999